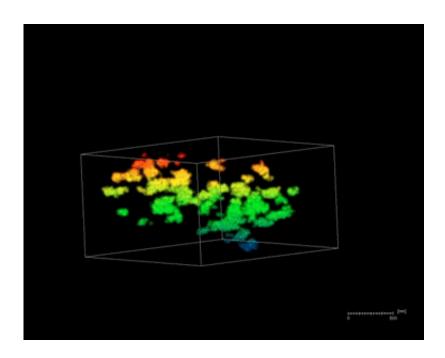


## Why some developing hearts can't tell left from right

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Credit: Yale University

When a developing heart can't tell left from right, it can take a team of scientists from a host of disciplines to explain why. Yale pediatricians, geneticists, cell biologists, and imaging experts have identified a surprising suspect that can send future heart cells in an embryo in the wrong directions, leading to a birth defect called heterotaxy.

A genetic analysis of a single infant born with such a malformed heart revealed a mutation in a gene called NUP188, which is a major



component of nuclear pore complexes that control molecular communication between the nucleus and cytoplasm of all cells. A defect in this complex should be lethal, so its presence in a living baby puzzled researchers.

Pediatrician Mustafa Khokha and colleagues found that frogs without NUP188 formed hearts with the same distorted left-right orientation as seen in the infant. Khokha then consulted with cell biologist, Patrick Lusk, who looked for evidence of NUP188 in other areas of the cell and found it at the bases of tiny hair-like structures projecting from the surface of cells called <u>cilia</u>.

Cilia, which enable mobility in many forms of <u>single cell organisms</u>, serve numerous purposes in animal cells—including generating fluid flow that directs cells to their proper locations in the developing embryo.

By applying a new three-dimensional super-resolution imaging technology recently developed by Joerg Bewersdorf's lab at Yale, NUP188 was visualized at the cilium base forming two large barrels (see accompanying image) that are unlike <u>nuclear pore complexes</u>. The researchers speculate that NUP188 plays a structural role at the bases of cilia. The paper was published Sept. 1 in the journal *Developmental Cell*.

## Provided by Yale University

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